

15A-B, in accordance with the identifiers appearing on the figures themselves. Support for such amendments to the figure references in the specification can be found in the figures themselves, as originally filed.

Claims 18-45, covering the non-elected subject matter, have been canceled without prejudice to the Applicants' right to pursue the subject matter of these claims in additional applications. Claims 1-17, covering the elected subject matter of Group I, are currently pending.

Claims 1-3 and 11-17, covering elected species A of Group I, are under active consideration.

Claims 1-3 have been amended to more particularly point out and distinctly claim that which Applicants regard as the invention. The amendments are fully supported in the specification. No new matter has been introduced.

Specifically, Claims 1 and 2 have been amended to specify peptides or small organic compounds. Support for such peptides or small organic compounds can be found, for example, at page 18, line 34; and page 29, lines 13-14.

Claim 2 has been amended, pursuant to the Examiner's suggestion, to specify the full name of the nucleoprotein, in lieu of the abbreviation NP. Support for nucleoprotein being the full name of NP can be found in the specification at page 1, line 22, and page 4, line 23, for example.

Claim 3 has been amended, pursuant to the Examiner's suggestion, to specify the full name of the nucleoprotein interactor-1, in lieu of the abbreviation NPI-1. Support for nucleoprotein interactor-1 being the full name of NPI-1 can be

found in the specification at page 8, lines 10-11, and page 34, line 6, for example.

The Claims Are Definite Under
35 U.S.C. § 112, Second Paragraph

Claims 1-3 and 11-17 have been rejected under 35 U.S.C. § 112, second paragraph as indefinite with respect to the term "receptor protein". The Examiner cites several medical dictionaries to assert that "there is no art recognized definition for the term" (Office Action, page 9).

Applicants respectfully disagree. In contrast to the Examiner's contention, the phrase "cell surface receptor" has a clear, definite meaning in the art of virology. Applicants direct the Examiner's attention to Chapter 12 of the well-known virology textbook, Fundamental Virology, Fields et al., eds. (Raven Press, 2nd ed. 1991). Chapter 12 of Fundamental Virology (pages 267-290), entitled "Virus Host Cell Interactions", by David M. Knipe, is submitted herewith in its entirety as Exhibit A (referred to hereinafter as "Knipe").

Knipe clearly articulates that, even though many different kinds of molecules can serve as cell-surface receptors, all cell-surface receptors are clearly defined by both their location and their function in viral infection. In the subsection entitled "Binding to Cell-Surface Receptors" (emphasis added), Knipe states:

The first event in viral infection of the host cell is binding of the virus to the cell surface. The cell-surface molecule with which the virus first interacts or binds is called the *cell receptor* (Knipe, page 269).

Regardless of the molecular characteristics of such cell-surface receptors, it is this functionally and spatially well defined class of molecules (which in the instant claims are further defined as proteins) which are intended to be excluded from the claims. In contrast, host cell proteins that participate in the intracellular events of viral infection, subsequent to the initial binding of the virus, are encompassed by the claims. For example, see the remainder of Knipe, which discusses viral entry, uncoating, and all subsequent events required for a productive infection. Applicant submits that a person of ordinary skill in the art of virology would clearly understand the distinction between these stages of viral infection. Therefore, the claims particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Applicants request, therefore, that the rejection of the claims under § 112, second paragraph with regard the phrase "receptor protein" be withdrawn.

Claims 1-3 and 11-17 have also been rejected under § 112, second paragraph as indefinite with respect to the phrase "amino acid sequence corresponding to" (Office Action, page 9). Specifically, the Examiner contends:

Possible interpretations of the phrase include amino acid sequences of the same length, the same amino acid composition or the same sequence. Since all of these are reasonable and distinct possibilities with very different consequences for the claimed assays, the skilled artisan would be confused as to what amino acid sequences are actually encompassed by the claims (Office Action, page 9).

Applicants respectfully submit that, in contrast to the Examiner's contention, the specification clearly sets forth

the meaning of such amino acid sequences corresponding to the binding site. Section 5.2.1. describes components of the claimed assays. In particular, peptide fragments are described which "correspond to the binding domains of the respective proteins" (page 20, lines 13-14). All the fragments are described as having the common property of "resulting in a functionally equivalent product" with respect to their ability to bind their binding partner (page 21, lines 11-12). Thus, a person of ordinary skill in the art would not, as the Examiner contends, be confused as to what amino acid sequences are encompassed by the claims. Rather the person of ordinary skill in the art would understand that the claims encompass amino acid sequences that bind each other in an equivalent manner to those of the corresponding natural proteins. Furthermore, these functionally equivalent sequences, by definition, would not have very different consequences on the claimed assays, in contrast to the Examiner's contention.

Therefore, the claims particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Applicants request, therefore, that the rejection of the claims under § 112, second paragraph with regard the phrase "amino acid sequence corresponding to" be withdrawn.

The rejections of Claims 2 and 3 under 35 U.S.C. § 112, second paragraph with respect to the recitation of the abbreviations for nucleoprotein and nucleoprotein inhibitor-1 have been obviated by the amendment replacing these

abbreviations with the full names of each respective protein, pursuant to the Examiner's suggestion.

The Claims Are Enabled Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 11-17 have been rejected under 35 U.S.C. § 112, first paragraph for lack of enablement (Office Action dated March 27, 1997, hereinafter "Office Action", pages 4-8). Specifically, the Examiner contends that the specification is not enabling for:

- a) 'any viral protein "required for viral infection, replication, assembly, or release"' (Office Action, page 4);
- b) 'any peptide or protein "corresponding to the binding site" of such proteins' (Office Action, page 5); and
- c) 'assays conducted "under conditions and for a time sufficient to permit binding and the formation of a complex"' (Office Action, page 7).

Regarding the phrase relating to viral proteins in item a), above, Applicants note that the claims exclude "cell surface receptor proteins". As explained in the discussion regarding the rejections under § 112, second paragraph, above, binding to such cell-surface receptor proteins is only the first step in the infection process.

The Examiner asserts that the art is unpredictable with respect to the three elements of the claims referred to in items a), b), and c), above. For example, the Examiner contends that:

While recombinant techniques are available, it is not routine in the art to screen large numbers of viral proteins where the expectation of obtaining similar binding activity/function is unpredictable based on the instant disclosure (Office Action, page 5, emphasis in original).

Applicants respectfully disagree.

First, the specification, in Section 5.2, and the examples whose results are summarized in Sections 6.2.3 and 7.2.3, for example, provide in detail the components and formats which readily enable one to detect protein-protein complex formation.

In addition to the explicit teachings of the specification, Applicants submit herewith, as Exhibit B, Phizicky & Fields, 1995, Microbiological Reviews 59: 94-123 (referred to hereinafter as "Phizicky"). Although Phizicky was published in March 1995, which is after the priority date of the present application (May 20, 1994), Applicants submit that, as a review article, it accurately reflects the general state of the art at the priority date of the instant application. Specifically, Phizicky clearly shows that basic techniques for identifying protein-protein interactions have become far advanced in the art.

As just one example, pages 105-106 provide a detailed overview of the interactive trap (*i.e.*, two-hybrid) system. In fact, Zervos et al., 1993, Cell 72: 223-232, cited in the specification at page 35, line 15 (full citation at page 34, lines 32-33) is also cited in Knipe (ref. 247, at page 105) as one of many methods for carrying out the two hybrid system. Applicant notes further that four of the additional references cited in the specification at page 40, line 4-8 are cited at

page 105 of Phizicky (Chien, et al., as ref. 35; Dalton & Treisman, as ref. 45; Durfee, et al., as ref. 55; and Vojtek, et al., as ref. 223).

Phizicky concludes with the following passage:

Ten to twenty years ago, only a few complexes of protein were well characterized as to their subunit compositions and specific interactions; currently, a large number of such complexes are known. Relatively soon, there may be an enormous number (Phizicky, page 118)

Thus, as Phizicky indicates, the art has met the challenge of identifying and characterizing various protein-protein interactions. Applicant submits that the specific teachings of the specification, in view of the general state of the art, enable the identification and characterization of a large number of protein-protein interactions -- including the amino acid sequences corresponding to protein-protein binding sites, and the conditions and time sufficient to permit binding and the formation of a complex. Therefore, the specification enables one skilled in the art to carry out the invention as claimed. Accordingly, Applicants request that the rejection for lack of enablement under § 112, first paragraph be withdrawn.

The Claims Are Novel Under 35 U.S.C. § 102

Claims 1, 11, 13, and 14 have been rejected under 35 U.S.C. § 102(b) as anticipated by Maddon et al., U.S. Patent No. 5,110,906. The Examiner has remarked that:

This rejection is based on a reasonably broad interpretation of the claims where the negative limitation comprising "receptor protein" is interpreted as having a narrow definition which excludes "receptors" that bind viruses (Office Action, page 10).

In view of the discussion of the rejection under 35 U.S.C. § 112, second paragraph, above, Applicants submit that Claim 1 (and Claims 11, 13, and 14 as dependent thereon) particularly and distinctly exclude from their scope cell-surface receptors that bind viruses. Thus, cell surface receptors such as T4 described in Maddon et al. are excluded from the claims. Therefore, Maddon et al. does not anticipate any of Claims 1, 11, 13, or 14. Applicants respectfully request, therefore, that the rejection under § 102 with respect to Maddon et al. be withdrawn.

Claim 1 has also been rejected under § 102(b) as being anticipated by Gannon et al., 1990, The New Biologist 2: 84-92. Applicants note that Claim 1 has been amended to specify a peptide or small organic compound. Gannon et al., on the other hand, report the use of antibodies to study the protein interactions of interest therein. Thus, the rejection of Claim 1 as anticipated by Gannon et al. has been obviated by the present amendment to Claim 1. Applicants request, therefore, that the rejection of Claim 1 under § 102(b) as anticipated by Gannon et al. be withdrawn.

Miscellaneous

Applicants note the Examiner's comments regarding the requirement of formal drawings should the application be allowed. Such formal drawings will be provided upon receipt of a Notice of Allowance. The references to Figures 2A-B, 8A-C, 12A-B, and 15A-B in the specification have been brought

into conformity with the figures themselves, as requested by the Examiner.

CONCLUSION

Applicant respectfully requests the entry of the foregoing amendments and remarks into the file of the above-captioned application. Applicant believes that each ground for rejection or objection has been successfully overcome or obviated and that the application is in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application is earnestly requested.

Respectfully submitted,

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